

REMARKS/ARGUMENTS

By this amendment, claims 57, 59-64, 66-83, 87-89, 92-93, 97-104, 109-110, and 113-169 are canceled without prejudice or disclaimer. Applicant intends to pursue the subject matter of these claims in one or more continuation and/or divisional applications. Claims 176-189 are currently pending the present application.

Rejection of claims 66, 69, 77, 93, 97, 116-118, 121-122, 124-125, 128, 131-136, and 162-169 under 35 USC §102(b) as anticipated by Eibl US Patent No. 5, 626,867

The Examiner has rejected claims 66, 69, 77, 93, 97, 116-118, 121-122, 124-125, 128, 131-136, and 162-169 under 35 USC §102(b) as anticipated by Eibl US Patent No. 5, 626,867. Applicant has canceled these claims without prejudice or disclaimer rendering this rejection moot. Applicant intends to pursue these claims in one or more divisional and/or continuation applications.

Rejection of claims 66-71, 73, 74, 76-83, 93, 97-103, 116-156, and 176-189 under 35 U.S.C. § 103(a) as obvious over Hristova, et al. Micromolecules, vol. 28, pp. 7693-7699, 1995 in combination with Ogawa et al. US Patent No. 5,094,854.

The Examiner has rejected claims 66-71, 73, 74, 76-83, 93, 97-103, 116-156, and 176-189 under 35 U.S.C. § 103(a) as obvious over Hristova, et al. Micromolecules, vol. 28, pp. 7693-7699, 1995 (hereinafter "Hristova") in combination with Ogawa et al. US Patent No. 5,094,854 (hereinafter "Ogawa"). Applicant respectfully requests reconsideration and withdrawal of this rejection.

Claims 66-71, 73, 74, 76-83, 93, 97-103, and 116-156 have been canceled. The following remarks will consider this rejection as applied to claims 176-189.

MPEP 2142 reads in pertinent part:

The key to supporting any rejection under 35 U.S.C. 103 is the clear articulation of the reason(s) why the claimed invention would have been obvious. The Supreme Court in *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___, ___, 82 USPQ2d 1385, 1396 (2007) noted that the analysis supporting a rejection under 35 U.S.C. 103 should be made explicit. The Federal Circuit has stated that "rejections on obviousness cannot be sustained with mere conclusory statements; instead, there must be some articulated

reasoning with some rational underpinning to support the legal conclusion of obviousness." In re Kahn, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006). See also KSR, 550 U.S. at ___, 82 USPQ2d at 1396 (quoting Federal Circuit statement with approval).

Applicant respectfully submits that the Examiner has not met his burden of supporting an obviousness rejection. In particular, the "differences between the prior art and the claims" must be considered. *KSR International Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1741 (2007) ("*KSR*") (quoting *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 17-18 (1966)). In addition, in *KSR* the U.S. Supreme Court acknowledged that "[o]ften, it will be necessary . . . to look to interrelated teachings of multiple patents . . . to determine whether there was an apparent reason to combine . . . elements in the fashion claimed . . . [But to] facilitate review, this analysis should be made explicit." *KSR*, 127 S. Ct. at 1741. (Emphasis added).¹

In a recent chemical case *Takeda Chem. Indus., v. Alphapharm Pty. Ltd.*, 492 F.3d 1350, 1356-57 (Fed. Cir. 2007) ("*Takeda*"), the Federal Circuit concurred with the reasoning in *KSR* while also emphasizing that there must be some identified reason that would have "prompted" a chemist to make a modification in a particular manner to establish *prima facie* obviousness. In *Takeda*, the Federal Circuit held, *inter alia*, that a person of ordinary skill in the art would not have been prompted to modify the closest prior art, using selective method steps, to achieve the claimed invention. 492 F.3d at 1350.

Independent claim 176, and claims 177-182 dependent thereon, require *inter alia* a liposome having a gel-phase bilayer membrane, comprising: (a) a first component which is dipalmitoylphosphatidylcholine (DPPC) in an amount ranging from 80 to 98 mol %; and (b) a second component selected from the group consisting of: (i) monostearoylphosphatidylcholine (MSPC) and 1,2-distearoyl-sn-glycero-3-phosphoethanolamine-N-[poly(ethyleneglycol) 2000]

¹ It is further noted that the Court in *KSR* discussed in some detail *United States v. Adams*, 383 U.S. 39 (1966) ("*Adams*"), stating in part that in *Adams*, "[t]he Court relied upon the corollary principle that when the prior art teaches away from combining certain known elements, discovery of a successful means of combining them is more likely to be nonobvious." (Citations omitted). (Emphasis added).

(DSPE-PEG-2000) in an amount ranging from 2 to 20 mol%; and (ii) monopalmitoylphosphatidylcholine (MPPC) and 1,2-distearoyl-sn-glycero-3-phosphoethanolamine-N-[poly(ethyleneglycol) 2000] (DSPE-PEG-2000) in an amount ranging from 2 to 20 mol%. Such liposomes are neither taught nor suggested by Hristova and Ogawa.

Independent claim 183, and claims 184-189 dependent thereon, require *inter alia* a liposome having a gel-phase bilayer membrane, comprising: (a) a first component which is dipalmitoylphosphatidylcholine (DPPC) in an amount ranging from 80 to 98 mol %; and (b) a second component selected from the group consisting of: (i) monostearoylphosphatidylcholine (MSPC) and 1,2-distearoyl-sn-glycero-3-phosphoethanolamine-N-[poly(ethyleneglycol) 2000] (DSPE-PEG-2000) in an amount ranging from 2 to 20 mol%; and (ii) monopalmitoylphosphatidylcholine (MPPC) and 1,2-distearoyl-sn-glycero-3-phosphoethanolamine-N-[poly(ethyleneglycol) 2000] (DSPE-PEG-2000) in an amount ranging from 2 to 20 mol%. Such liposomes are neither taught nor suggested by Hristova and Ogawa.

The Examiner asserts that Hristova discloses liposomal formulations containing dipalmitoylphosphatidylcholine and a lysolipid. Final Office Action, page 3. Applicant disagrees with this characterization of the disclosure of Hristova. The lysolipid-containing liposome disclosed by Hristova at page 7697 right column last paragraph comprises POPE-PEG (1-palmitoyl 2-oleoylphosphatidylethanolamine-PEG), EPC (egg phosphatidylcholine), and MOPC (mono-oleoylphosphatidylcholine). This is the only lysolipid-containing liposome disclosed by Hristova. The Examiner goes on to assert "it would have been obvious to one of ordinary skill in the art to use any lysophosphatidylcholine (that is substituted with any fatty acid moiety) with the expectation of obtaining similar effect on the gel phase bilayers." Final Office Action, page 3.

Applicant would like to point out that this assertion is exactly the type of conclusory statement referred to above and not the motivation, or explicit indications that one would have prompted one of skill in the art to modify the reference in the manner presently claimed. In fact, the Office's assertions contravene the explicit disclosure of the references.

The liposomes of Hristova differ from the presently claimed liposomes in at least three ways. First, Hristova describes a liposome comprising POPE-PEG:EPC:MOPC, and one of ordinary skill in the art would understand that EPC (egg phosphatidylcholine) forms a liquid crystalline bilayer, not a gel-phase bilayer. Second, the liposomes disclosed by Hristova lack the presently claimed lysolipid. Third, the liposomes of Hristova do not comprise the presently claimed ratios of components. The liposomes of Hristova comprise a 1:1 ratio of POPE-PEG and EPC to MOPC. Hristova page 7697 right column last paragraph. Therefore, the Hristova disclosure, as a whole, is entirely different from the claimed invention. See *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), cert. denied, 469 U.S. 851 (1984) (indicating that prior art references must be considered in their entirety, as a whole, including any disclosures that lead away from the claims at issue).

The deficiencies of Hristova are not cured by Ogawa. Ogawa discloses a liposomal membrane that includes specific phospholipids. See column 3, lines 16-20 and the Examples of Ogawa, which indicate a combination of only DPPC and DSPC in a liposomal membrane. Ogawa does not disclose the use of any lysolipid and, therefore, does not disclose the presently claimed lysolipid. Further, Ogawa does not disclose the presently claimed ratios of components. Accordingly, Ogawa clearly does not cure the deficiencies of Hristova.

Applicant respectfully submits that the Examiner has failed to present a *prima facie* case for the obviousness of the claimed invention. Accordingly, Applicant respectfully requests reconsideration and withdrawal of this rejection.

Double Patenting Rejection

Claims 66-71, 73, 74, 76-83, 93, 97-103, 116-156 and 159-169, 176-189 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-68 of U.S. Patent No. 6,726,925.

Applicant will submit a terminal disclaimer to obviate this rejection when the Examiner indicates the claims are allowable.

Conclusion

In view of the above amendments and remarks, Applicant believes the pending application is in condition for allowance. An expedited notification of allowance is kindly requested. If, however, there are any issues that the Examiner would like to discuss, the Examiner is invited to contact Applicant's representative at the number listed below.

Applicant believe no fee is due with this response. However, the Commissioner is hereby authorized in this, concurrent, and further replies, to charge payment or credit any overpayment to Deposit Account No. 22-0185, under Order No. 14514-00007-US1 from which the undersigned is authorized to draw.

Dated: February 26, 2008

Respectfully submitted,

Electronic signature: /Lawrence J. Carroll/
Lawrence J. Carroll
Registration No.: 40,940
CONNOLLY BOVE LODGE & HUTZ LLP
1875 Eye Street, NW
Suite 1100
Washington, DC 20006
(202) 331-7111
(202) 293-6229 (Fax)
Attorney for Applicant

72736v1